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EPO, and German patents  
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=> s futhan/cn

L1 1 FUTHAN/CN

=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS

RN 82956-11-4 REGISTRY

CN Benzoic acid, 4-[(aminoiminomethyl)amino]-, 6-(aminoiminomethyl)-2-naphthalenyl ester, dimethanesulfonate (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 6-Amidino-2-naphthyl p-guanidinobenzoate

CN FUT 175

CN **Futhan**

CN Nafamostat mesilate

CN Nafamostat mesylate

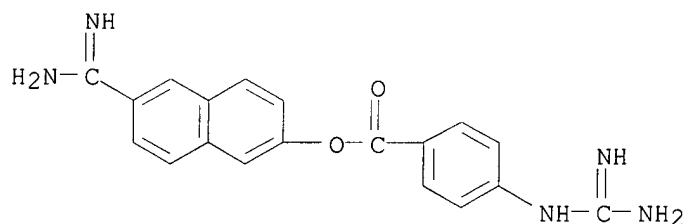
MF C19 H17 N5 O2 . 2 C H4 O3 S

LC STN Files: ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CBNB, CIN, DDFU, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IMSDIRECTORY, IPA, MRCK\*, PHAR, PROMT, RTECS\*, TOXLINE, TOXLIT, USAN, USPATFULL  
(\*File contains numerically searchable property data)

CM 1

CRN 81525-10-2

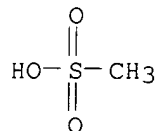
CMF C19 H17 N5 O2



CM 2

CRN 75-75-2

CMF C H4 O3 S



204 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

206 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus, uspatfull, biosis, medline

COST IN U.S. DOLLARS

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FILE 'CAPLUS' ENTERED AT 10:48:29 ON 07 MAR 2000

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FILE 'USPATFULL' ENTERED AT 10:48:29 ON 07 MAR 2000

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FILE 'BIOSIS' ENTERED AT 10:48:29 ON 07 MAR 2000

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FILE 'MEDLINE' ENTERED AT 10:48:29 ON 07 MAR 2000

=> s 11

L2 338 L1

=> s ?cardio? or ?heart?

L3 1915003 ?CARDIO? OR ?HEART?

=> s 12 and 13

L4 48 L2 AND L3

=> s 12 (P) 13

L5 5 L2 (P) L3

=> dup rem 14

PROCESSING COMPLETED FOR L4

L6 45 DUP REM L4 (3 DUPLICATES REMOVED)

=> d 1-5 bib,ab 15

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2000 ACS

AN 1998:12232 CAPLUS

DN 128:86085

TI Elimination of Kupffer cells and administration of protease inhibitor  
improve graft viability and prevent reperfusion injury in NHBD

AU Tsukamoto, S.; Ohkohchi, N.; Orii, T.; Fukumori, T.; Asakura, T.;  
Takayama, J.; Kato, H.; Satomi, S.

CS Second Dep. Surgery, Tohoku Univ. School Medicine, Sendai, Japan

SO Transplant. Proc. (1997), 29(8), 3463-3464

CODEN: TRPPA8; ISSN: 0041-1345

PB Elsevier Science Inc.

DT Journal

LA English

AB The aim of this study was to det. whether liver grafts from  
non-heartbeating donors are suitable for clin. liver transplantation.

The authors report that the elimination of Kupffer cells and administration  
of

NM (nafamostat mesilate), a serine protease inhibitor that inhibits  
phospholipase A2, improves graft viability and prevents reperfusion  
injury

in non-heartbeating donors.

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2000 ACS

AN 1998:183 CAPLUS

DN 128:110669

TI Effects of protease inhibitors on postischemic recovery of the heart

AU Shibata, Toshihiko; Yamamoto, Fumio; Suehiro, Shigefumi; Kinoshita, Hiroaki

CS Second Dep. of Surgery, Osaka City University Medical School, Osaka, 545, Japan

SO Cardiovasc. Drugs Ther. (1997), 11(4), 547-556

CODEN: CDTKET; ISSN: 0920-3206

PB Kluwer Academic Publishers

DT Journal

LA English

AB It is well known that activation of proteases in the lysosomes and cytosol

is one of the mechanisms of ischemic injury. It might thus be beneficial to det. whether the addn. of several clin. available protease inhibitors to a cardioplegic soln. can improve its protective ability. Using an isolated working rat heart prepn., the effects of several protease inhibitors (serine protease inhibitors; nafamostat mesylate and gabexate mesylate, a thiol-protease inhibitor; NCO-700; and a urinary trypsin inhibitor, urinastatin) on the postischemic recovery of function and enzyme leakage were investigated in this study. These protease inhibitors

were added to either the cardioplegic soln. or reperfusion soln. The addn. of each of the protease inhibitors, except urinastatin, to the cardioplegic soln. improved the postischemic recovery of function and reduced enzyme leakage. The dose-response characteristics of these three protease inhibitors were bell shaped, and the optimal concns. of nafamostat mesylate, gabexate mesylate, and NCO-700 were 5 .mu.M, 100 .mu.M, and 20 .mu.M, resp. In contrast to the results of the preischemic treatment study, the addn. of any of the protease inhibitors to the perfusion medium during Langendorff reperfusion failed to improve the postischemic recovery of function and to reduce enzyme leakage. Surprisingly, the addn. of NCO-700 to the reperfusion soln. at a concn.

of 5 .mu.M or higher had rather harmful effects on both functional recovery and enzyme leakage. These findings suggest that serine and thiol proteases may play an important role in myocardial injury during ischemia, but not necessarily during reperfusion.

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2000 ACS

AN 1997:31579 CAPLUS

DN 126:84283

TI The effect and pharmacokinetics of nafamostat mesilate adjunct to cold nondepolarizing cardioplegia in a canine model of cardiac preservation

AU Sunamori, Makoto; Yoshida, Tetsuya; Miyamoto, Hisashi; Wang, Yigang; Suzuki, Akio

CS School Medicine, Tokyo Medical and Dental University, Tokyo, 113, Japan

SO Transplant Int. (1996), 9(4), 364-369

CODEN: TRINE5; ISSN: 0934-0874

PB Springer

DT Journal

LA English

AB The effects of nafamostat mesilate (NM) on myocardial, biochem., and functional changes in canine hearts were examd. An isolated heart was preserved for 6 h at 5.degree. and then reperfused for 2 h at 37.degree.. NM was added to the cardioplegic soln. At both 10-7M and 10-6M, NM was able to maintain myocardial cAMP at a normal level and to reduce cGMP concns. at the end of both preservation and reperfusion. The serum N-acetyl-.beta.-D-glucosaminidase concn. during reperfusion was lower in hearts treated with NM 10-6 or 10-7M NM than in those without NM. Although NM failed to preserve myocardial concns. of adenine nucleotide compds., NM at 10-7M maintained the .+-. dp/dt of the left ventricle

after

reperfusion at same level as in the nonischemic control group and better than NM at 10-6M or no NM. Myocardial uptake of 10-5M NM was 55% during the 6-h preservation and 29% during the 2-h reperfusion. It is concluded that addn. of 10-7M NM to a nondepolarizing soln. does not preserve myocardial adenine nucleotide concns. but does facilitate the recovery of left ventricular function. NM at 10-5M seems to have a high affinity for the myocardium and may depress the recovery of left ventricular function.

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2000 ACS  
AN 1993:404342 CAPLUS  
DN 119:4342  
TI Efficacy of futhan rinse solution following rat heart preservation  
AU Urushihara, Takashi; Sumimoto, Kazuo; Sumimoto, Ryo; Ikeda, Masanobu; Fukuda, Yasuhiko; Dohi, Kiyohiko  
CS Sch. Med., Hiroshima Univ., Hiroshima, Japan  
SO Nippon Geka Gakkai Zasshi (1992), 93(12), 1514  
CODEN: NGGZAK; ISSN: 0301-4894  
DT Journal  
LA Japanese  
AB The efficacy of futhan rinse soln. following rat heart preservation was studied and compared with that of physiol. saline soln. and Carolina Rinse-II soln. The graft survival after 18-h preservation was 100, 50, and 50% in futhan rinse, physiol. saline, and Carolina Rinse-II group, resp. These results suggest the potential of clin. application of futhan rinse soln.

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2000 ACS  
AN 1989:546489 CAPLUS  
DN 111:146489  
TI Experimental study on the usefulness of the protease inhibitor, nafamostat mesilate (FUT), as an anticoagulant in left heart bypass  
AU Saito, A.; Moro, H.; Eguchi, S.; Yokosawa, T.  
CS Sch. Med., Niigata Univ., Niigata, Japan  
SO Jinko Zoki (1989); 18(2), 453-6  
CODEN: JNZKA7; ISSN: 0300-0818  
DT Journal  
LA Japanese  
AB The left heart bypass was performed in seven mongrel dogs for 4 h using a protease inhibitor nafamostat mesilate (FUT) as an anticoagulant. Bypass flow was 200 mL/min (20% of cardiac output) and FUT was infused continuously via the inflow cannula. ACT (activated clotting time), platelet counts, activated partial thrombin time and fructose 1,6-diphosphate were measured during the bypass. The results show that nafamostat mesilate is a useful and safe anticoagulant for mech. circulatory support.

=>

=> d 16 1-45 bib

L6 ANSWER 1 OF 45 CAPLUS COPYRIGHT 2000 ACS  
AN 1999:595348 CAPLUS  
DN 131:225828  
TI Methods of diagnosis and triage using cell activation measures  
IN Stoughton, Roland B.; Schmid-Schonbein, Geert W.; Hugli, Tony E.; Kistler, Erik  
PA Cell Activation, Inc., USA; The Regents of the University of California; The Scripps Research Institute  
SO PCT Int. Appl., 184 pp.  
CODEN: PIXXD2  
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9946367	A2	19990916	WO 1999-US5247	19990311
	WO 9946367	A3	19991209		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9931829	A1	19990927	AU 1999-31829	19990311
PRAI	US 1998-38894		19980311		
	WO 1999-US5247		19990311		
L6	ANSWER 2 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS				
AN	1999:200615 BIOSIS				
DN	PREV199900200615				
TI	Prevention of neointimal formation by a serine protease inhibitor, FUT-175, after carotid balloon injury in rats.				
AU	Sawada, Motoshi; Yanamoto, Hiroji (1); Nagata, Izumi; Hashimoto, Nobuo; Nakahara, Ichiro; Akiyama, Yoshinori; Kikuchi, Haruhiko				
CS	(1) Laboratory for Cerebrovascular Disorders, National Cardio-Vascular Center Research Institute, 5-7-1 Fujishiro-dai, Suita, 565-8565 Japan				
SO	Stroke, (March, 1999) Vol. 30, No. 3, pp. 644-650. ISSN: 0039-2499.				
DT	Article				
LA	English				
L6	ANSWER 3 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS				
AN	1999:470874 BIOSIS				
DN	PREV199900470874				
TI	Direct evidence of the role of mucosal mast cell activation in the pathogenesis of intestinal ischemia-reperfusion injury in rats.				
AU	Kimura, T. (1); Andoh, A. (1); Fukuda, M. (1); Tsujikawa, T. (1); Sasaki, M. (1); Fujiyama, Y. (1); Bamba, T. (1)				
CS	(1) Dept. of Internal Medicine, Shiga University of Medical Science, Otsu Japan				
SO	Journal of Parenteral and Enteral Nutrition, (Sept. Oct., 1999) Vol. 23, No. 5 SUPPL., pp. S149. Meeting Info.: International Symposium on Growth Factors and Nutrients in Intestinal Health and Disease Osaka, Japan October 31-November 3, 1998 ISSN: 0148-6071.				
DT	Conference				
LA	English				
L6	ANSWER 4 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS				
AN	1998:475040 BIOSIS				
DN	PREV199800475040				
TI	Interleukin-6 derived from hypoxic myocytes promotes neutrophil-mediated reperfusion injury in myocardium.				
AU	Sawa, Yoshiki (1); Ichikawa, Hajime; Kagisaki, Koji; Ohata, Toshihiro; Matsuda, Hikaru				
CS	(1) First Dep. Surg., Osaka Univ. Med. Sch., 2-2 Yamada-oka, Suita, Osaka 565 Japan				
SO	Journal of Thoracic and Cardiovascular Surgery, (Sept., 1998) Vol. 116, No. 3, pp. 511-517. ISSN: 0022-5223.				
DT	Article				
LA	English				
L6	ANSWER 5 OF 45 CAPLUS COPYRIGHT 2000 ACS				

AN 1998:12232 CAP  
DN 128:86085  
TI Elimination of Kupffer cells and administration of protease inhibitor  
improve graft viability and prevent reperfusion injury in NHBD  
AU Tsukamoto, S.; Ohkohchi, N.; Orii, T.; Fukumori, T.; Asakura, T.;  
Takayama, J.; Kato, H.; Satomi, S.  
CS Second Dep. Surgery, Tohoku Univ. School Medicine, Sendai, Japan  
SO Transplant. Proc. (1997), 29(8), 3463-3464  
CODEN: TRPPA8; ISSN: 0041-1345  
PB Elsevier Science Inc.  
DT Journal  
LA English

L6 ANSWER 6 OF 45 CAPLUS COPYRIGHT 2000 ACS  
AN 1998:183 CAPLUS  
DN 128:110669  
TI Effects of protease inhibitors on postischemic recovery of the  
heart  
AU Shibata, Toshihiko; Yamamoto, Fumio; Suehiro, Shigefumi; Kinoshita,  
Hiroaki  
CS Second Dep. of Surgery, Osaka City University Medical School, Osaka, 545,  
Japan  
SO Cardiovasc. Drugs Ther. (1997), 11(4), 547-556  
CODEN: CDTHET; ISSN: 0920-3206  
PB Kluwer Academic Publishers  
DT Journal  
LA English

L6 ANSWER 7 OF 45 USPATFULL  
AN 96:94448 USPATFULL  
TI Perfusion and storage solution containing sodium lactobionate, sodium  
dihydrogenphosphate, raffinose, glutathione, allopurinol and nafamostat  
mesylate  
IN Dohi, Kiyohiko, Hiroshima, Japan  
Urushihara, Takashi, Hiroshima, Japan  
Iwata, Masanori, Chiba, Japan  
PA Torii Pharmaceutical Co., Ltd., Tokyo, Japan (non-U.S. corporation)  
PI US 5565317 19961015  
WO 9400008 19940106  
AI US 1994-347490 19941206 (8)  
WO 1993-JP219 19930223  
19941206 PCT 371 date  
19941206 PCT 102(e) date  
PRAI JP 1992-168977 19920626  
DT Utility  
EXNAM Primary Examiner: Naff, David M.; Assistant Examiner: Saucier, S.  
LREP Beveridge, DeGrandi, Weilacher & Young, L.L.P.  
CLMN Number of Claims: 17  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 263  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 8 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1996:321861 BIOSIS  
DN PREV199699044217  
TI Pharmacological therapeutic prospects of cerebral vasospasm.  
AU Hans, P.  
CS Serv. Univ. d'Anesthesie Reanim., CHR de la Citadelle, 4000 Liege Belgium  
SO Annales Francaises d'Anesthesie et de Reanimation, (1996) Vol. 15, No. 3,  
pp. 374-381.  
ISSN: 0750-7658.  
DT General Review  
LA French  
SL French; English

L6 ANSWER 9 OF 45 CAPLUS COPYRIGHT 2000 ACS  
 AN 1997:31579 CAPLUS  
 DN 126:84283  
 TI The effect and pharmacokinetics of nafamostat mesilate adjunct to cold nondepolarizing **cardioplegia** in a canine model of cardiac preservation  
 AU Sunamori, Makoto; Yoshida, Tetsuya; Miyamoto, Hisashi; Wang, Yigang; Suzuki, Akio  
 CS School Medicine, Tokyo Medical and Dental University, Tokyo, 113, Japan  
 SO Transplant Int. (1996), 9(4), 364-369  
 CODEN: TRINE5; ISSN: 0934-0874  
 PB Springer  
 DT Journal  
 LA English

L6 ANSWER 10 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
 AN 1996:408501 BIOSIS  
 DN PREV199699130857  
 TI Effect of FUT-175 on postoperative organ dysfunction following open **heart** surgery with **cardiopulmonary** bypass (with special reference to soluble adhesion molecules.  
 AU Shimamoto, A. (1); Sato, T.; Kondo, C.; Shomura, Y. (1); Hioki, I. (1); Tempaku, H. (1); Maze, Y. (1); Takao, M. (1); Onoda, K.; Tani, K.; Tanaka, K.; Shimo, H.; Yada, I.  
 CS (1) Dep. Thorac. and CV Surg., Mie Univ. Sch. Med., 2-174 Edobashi, Tsu, Mie 514 Japan  
 SO Japanese Journal of Artificial Organs, (1996) Vol. 25, No. 2, pp. 361-364.  
 ISSN: 0300-0818.  
 DT Article  
 LA Japanese  
 SL Japanese; English

L6 ANSWER 11 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
 AN 1997:33421 BIOSIS  
 DN PREV199799339824  
 TI Investigation of the anti-complement agents, FUT-175 and K76COOH, in discordant xenotransplantation.  
 AU Kobayashi, T.; Neethling, F. A.; Taniguchi, S.; Ye, Y.; Niekrasz, M.; Koren, E.; Hancock, W. W.; Takagi, H.; Cooper, D. K. C. (1)  
 CS (1) Transplantation Biology Res. Cent., Mass. General Hosp., MGH-East, Boston, MA 02129 USA  
 SO Xenotransplantation, (1996) Vol. 3, No. 3, pp. 237-245.  
 ISSN: 0908-665X.  
 DT Article  
 LA English

L6 ANSWER 12 OF 45 CAPLUS COPYRIGHT 2000 ACS  
 AN 1996:105043 CAPLUS  
 DN 124:193852  
 TI Nafamostat mesylate, a broad spectrum protease inhibitor, modulates platelet, neutrophil and contact activation in simulated extracorporeal circulation  
 AU Sundaram, Sumuk; Gikakis, Nicolas; Hack, C. Erik; Niewiarowski, Stefan; Edmunds, L. H., Jr.; Rao, A. Koneti; Sun, Ling; Cooper, S. L.; Colman, Robert W.  
 CS Sol Sherry Thrombosis Res. Cent., Temple Univ. Sch. Med., Philadelphia, PA, 19140, USA  
 SO Thromb. Haemostasis (1996), 75(1), 76-82  
 CODEN: THHADQ; ISSN: 0340-6245  
 DT Journal  
 LA English

L6 ANSWER 13 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
 AN 1996:112706 BIOSIS



DN PREV199698684841  
TI Attenuation of **cardiopulmonary** bypass-derived inflammatory reactions reduces myocardial reperfusion injury in cardiac operations.  
AU Sawa, Yoshiki; Shimazaki, Yasuhisa; Kadoba, Keishi; Masai, Takashi; Fukuda, Hirotsugu; Ohata, Toshihiro; Taniguchi, Kazuhiro; Matsuda, Hikaru (1)  
CS (1) First Dep. Surgery, Osaka Univ. Med. Sch., 2-2 Yamada-oka, Suita, Osaka 565 Japan  
SO Journal of Thoracic and Cardiovascular Surgery, (1996) Vol. 111, No. 1, pp. 29-35.  
ISSN: 0022-5223.  
DT Article  
LA English

L6 ANSWER 14 OF 45 USPTAFULL  
AN 95:45354 USPTAFULL  
TI Thermoplastic polymer composition and medical devices made of the same  
IN Endo, Fumiaki, Fuji, Japan  
Saiga, Nobuko, Hadano, Japan  
PA Terumo Kabushiki Kaisha, Tokyo, Japan (non-U.S. corporation)  
PI US 5417981 19950523  
AI US 1993-53499 19930428 (8)  
PRAI JP 1992-136329 19920428  
DT Utility  
EXNAM Primary Examiner: Kight, III, John; Assistant Examiner: Dodson, Shelley A.  
LREP Burns, Doane, Swecker & Mathis  
CLMN Number of Claims: 24  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 489  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 15 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1996:142434 BIOSIS  
DN PREV199698714569  
TI Nafamostat mesylate is the first choice anticoagulant for continuous renal replacement therapy.  
AU Sugai, Takao; Hirasawa, Hiroyuki; Ohtake, Yoshio; Oda, Shigeto; Nakanishi, Kazuya; Kitamura, Nobuya; Matsuda, Kenichi; Kawabe, Touichi; Ueno, Hirokazu; Touma, Takayuki; Yokohari, Kenji  
CS Dep. Emergency, Critical Care Med., Chiba Univ. Sch. Med., Chiba Japan  
SO Blood Purification, (1995) Vol. 13, No. 6, pp. 388.  
Meeting Info.: International Conference on Continuous Renal Replacement Therapies San Diego, California, USA November 8-10, 1995  
ISSN: 0253-5068.  
DT Conference  
LA English

L6 ANSWER 16 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1995:243942 BIOSIS  
DN PREV199598258242  
TI The anti-complement effects of FUT-175 on myocardial ischemia/reperfusion injury in the blood-perfused isolated rabbit **hearts**.  
AU Yokota, Syunji (1); Kan-No, Satoshi; Saitoh, Yoshiaki; Kasama, Kikuko; Ohara, Naoki; Ono, Hiroshi  
CS (1) Lab. Applied Pharmacology, Hatano Res. Inst., Food Drug Safety Center, Kanagawa 257 Japan  
SO Japanese Journal of Pharmacology, (1995) Vol. 67, No. SUPPL. 1, pp. 280P.  
Meeting Info.: 68th Annual Meeting of the Japanese Pharmacological Society  
Nagoya, Japan March 25-28, 1995

DT ISSN: 0021-5198  
LA Conference  
English

L6 ANSWER 17 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1995:257247 BIOSIS  
DN PREV199598271547  
TI Inhibitory effect of FUT-175 on the production of interleukin 8 and  
polymorphonuclear leukocyte elastase.  
AU Kikuchi, Mitsuru (1); Endo, Shigeatsu; Inada, Katsuya; Yamashita,  
Hisahiko; Takauwa, Tetsuya; Nakae, Hajime; Kasai, Takeshi; Baba, Nobuo;  
Yamada, Yasuhiko  
CS (1) Critical Care Emergency Cent., Iwate Med. Univ., 19-1 Uchimaru,  
Morioka 020 Japan  
SO Research Communications in Molecular Pathology and Pharmacology, (1995)  
Vol. 87, No. 3, pp. 269-274.  
DT Article  
LA English

L6 ANSWER 18 OF 45 CAPLUS COPYRIGHT 2000 ACS  
AN 1994:129080 CAPLUS  
DN 120:129080  
TI Organ-preserving fluid  
IN Dohi, Kiyohiko; Urushihara, Takashi; Iwata, Masanori  
PA Torii and Co., Ltd., Japan  
SO PCT Int. Appl., 13 pp.  
CODEN: PIXXD2  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9400008	A1	19940106	WO 1993-JP219	19930223
	W: AU, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9335749	A1	19940124	AU 1993-35749	19930223
	AU 664074	B2	19951102		
	EP 647398	A1	19950412	EP 1993-904336	19930223
	EP 647398	B1	19970917		
	R: DE, FR, GB				
	US 5565317	A	19961015	US 1994-347490	19941206
PRAI	JP 1992-168977	19920626			
	WO 1993-JP219	19930223			

L6 ANSWER 19 OF 45 USPATFULL  
AN 94:71052 USPATFULL  
TI Gas permeable thrombo-resistant coatings and methods of manufacture  
IN Winters, Suzanne, Salt Lake City, UT, United States  
Solen, Kenneth A., Orem, UT, United States  
Sanders, Clifton G., Salt Lake City, UT, United States  
Mortensen, JD, Sandy, UT, United States  
Berry, Gaylord, Salt Lake City, UT, United States  
PA Cardiopulmonics, Inc., Salt Lake City, UT, United States (U.S.  
corporation)  
PI US 5338770 19940816  
AI US 1990-509063 19900412 (7)  
DCD 20101116  
RLI Continuation-in-part of Ser. No. US 1988-215014, filed on 5 Jul 1988,  
now patented, Pat. No. US 5262451 which is a continuation-in-part of  
Ser. No. US 1988-204115, filed on 8 Jun 1988, now patented, Pat. No. US  
4850958  
DT Utility  
EXNAM Primary Examiner: Szekely, Peter  
LREP Workman Nydegger Jensen  
CLMN Number of Claims: 33  
ECL Exemplary Claim: 1

- L6 ANSWER 20 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1995:67714 BIOSIS  
DN PREV199598082014  
TI Platelet protection with FUT-175 during **cardiopulmonary** bypass surgery: Electron microscopic study.  
AU Takagi, K.; Kondo, C.; Tanaka, K.; Yada, I.; Kusagawa, M.  
CS Dep. Thorac. Surg., Mie Univ. Sch. Med., 2-174 Edobashi, Tsu, Mie 514 Japan  
SO Japanese Journal of Artificial Organs, (1994) Vol. 23, No. 5, pp. 1089-1094.  
ISSN: 0300-0818.  
DT Article  
LA Japanese  
SL Japanese; English
- L6 ANSWER 21 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1994:384344 BIOSIS  
DN PREV199497397344  
TI Cardiac xenotransplantation from pig to Japanese monkey with splenectomy, tacrolims, filtration plasmapheresis, and nafamstat mesilate.  
AU Kawauchi, M. (1); Takeda, M.; Nakajima, J.; Matsumoto, J.; Furuse, A.  
CS (1) Dep. Thoracic Surg., Univ. Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113 Japan  
SO Transplantation Proceedings, (1994) Vol. 26, No. 3, pp. 1076-1077.  
Meeting Info.: Second International Congress on Xenotransplantation  
Cambridge, England, UK September 26-29, 1993  
ISSN: 0041-1345.  
DT Conference  
LA English
- L6 ANSWER 22 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1995:24486 BIOSIS  
DN PREV199598038786  
TI Effects of protease inhibitor and immunosuppressant on cerebral vasospasm after subarachnoid hemorrhage in rabbits.  
AU Yanamoto, Hiroji; Kikuchi, Haruhiko (1); Okamoto, Shinichiro  
CS (1) Dep. Neurosurg., Kyoto Univ. Med. Sch., Kawahara 54 Syogoin, Sakyo, Kyoto 606 Japan  
SO Surgical Neurology, (1994) Vol. 42, No. 5, pp. 382-387.  
ISSN: 0090-3019.  
DT Article  
LA English
- L6 ANSWER 23 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1995:24485 BIOSIS  
DN PREV199598038785  
TI Cerebral vasospasm caused by cisternal injection of polystyrene latex beads in rabbits is inhibited by a serine protease inhibitor.  
AU Yanamoto, Hiroji; Kikuchi, Haruhiko (1); Okamoto, Shinichiro; Nozaki, Kazuhiko  
CS (1) Dep. Neurosurg., Kyoto Univ. Med. Sch., Kawahara 54, Syogoin, Sakyo, Kyoto 606 Japan  
SO Surgical Neurology, (1994) Vol. 42, No. 5, pp. 374-381.  
ISSN: 0090-3019.  
DT Article  
LA English
- L6 ANSWER 24 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1994:191784 BIOSIS  
DN PREV199497204784  
TI Effect of nafamostat mesilate on Bradykinin generation and hemodynamic changes during LDL apheresis.

AU Kojima, S. (1); Chiba-Harada, M.; Nomura, S.; Kurochi, M.; Yamamoto, A.  
 CS (1) Tohsei Natl Hosp. Japan  
 SO Artificial Organs, (1994) Vol. 18, No. 2, pp. 138.  
 Meeting Info.: 5th International Congress of the World Apheresis  
 Association Houston, Texas, USA March 9-12, 1994  
 ISSN: 0160-564X.  
 DT Conference  
 LA English

L6 ANSWER 25 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
 AN 1994:293247 BIOSIS  
 DN PREV199497306247  
 TI Effect of FUT-175 (nafamostat mesilate) on the development of shock.  
 AU Maekawa, Yuriko; Koshiyama, Yoshiko; Kashiwabara, Sanae; Oda, Minoru;  
 Iwaki, Masahiro  
 CS Res. Lab., Torii and Co. Ltd., Chiba 267 Japan  
 SO Japanese Journal of Pharmacology, (1994) Vol. 64, No. SUPPL. 1, pp. 97P.  
 Meeting Info.: 67th Annual Meeting of the Japanese Pharmacological  
 Society  
 Kyoto, Japan March 21-24, 1994  
 ISSN: 0021-5198.  
 DT Conference  
 LA English

L6 ANSWER 26 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
 AN 1993:533727 BIOSIS  
 DN PREV199345120821  
 TI Nafamostat mesilate reduces postoperative blood loss in open heart  
 surgery.  
 AU Murase, M.; Maeda, M.; Teranishi, K.; Sakurai, H.; Nishizawa, T.; Koyama,  
 T.; Itoh, T.  
 CS Ohgaki Municipal Hosp., Dep. thoracic Surg., 4-86 Minaminokawa, Ohggaki,  
 Gifu 503 Japan  
 SO Japanese Journal of Artificial Organs, (1993) Vol. 22, No. 3, pp.  
 943-946.  
 Meeting Info.: Thirtieth Meeting of the Japanese Society for Artificial  
 Organs  
 ISSN: 0300-0818.  
 DT Article  
 LA Japanese  
 SL Japanese; English

L6 ANSWER 27 OF 45 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1  
 AN 1993:508660 CAPLUS  
 DN 119:108660  
 TI Prolonging discordant xenograft survival with anticomplement reagents  
 K76COOH and FUT175  
 AU Miyagawa, Shuji; Shirakura, Ryota; Matsumiya, Goro; Fukushima, Norihide;  
 Nakata, Seizoh; Matsuda, Hikaru; Matsumoto, Misako; Kitamura, Hajime;  
 Seya, Tsukasa  
 CS Med. Sch., Osaka Univ., Osaka, 553, Japan  
 SO Transplantation (1993), 55(4), 709-13  
 CODEN: TRPLAU; ISSN: 0041-1337  
 DT Journal  
 LA English

L6 ANSWER 28 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
 AN 1993:392414 BIOSIS  
 DN PREV199396067714  
 TI Effect of nafamostat mesilate on sodium and potassium transport  
 properties  
 in the rabbit cortical collecting duct.  
 AU Muto, Shigeaki (1); Imai, Masashi; Asano, Yasushi  
 CS (1) Dep. Nephrol. Pharmacol., Jichi Med. Sch., 3311-1 Minamikawachi,  
 Tochigi 329-04 Japan  
 SO British Journal of Pharmacology, (1993) Vol. 109, No. 3, pp. 673-678.

ISSN: 0007-1188  
DT Article  
LA English

L6 ANSWER 29 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1993:413296 BIOSIS  
DN PREV199396079021  
TI Nafamostat mesilate: A regional anticoagulant for hemodialysis in patients at high risk for bleeding.  
AU Akizawa, Tadao (1); Koshikawa, Shozo; Ota, Kazuo; Kazama, Mutsuyoshi; Mimura, Nobuhide; Hirasawa, Yoshihei  
CS (1) Dep. Internal Med., Showa Univ., Fujigaoka Hosp., 1-30 Fujigaoka, Midori-ku, Yokohama 227 Japan  
SO Nephron, (1993) Vol. 64, No. 3, pp. 376-381.  
ISSN: 0028-2766.  
DT Article  
LA English

L6 ANSWER 30 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1993:220149 BIOSIS  
DN PREV199344104649  
TI Intravenous FUT-175 inhibits complement activation in the cerebrospinal fluid and vasospasm-related delayed ischemic neurological deficit following subarachnoid hemorrhage.  
AU Yanamoto, H. (1); Kikuchi, H. (1); Okamoto, S.; Ishikawa, J.; Matsumoto, M.; Shimizu, Y.; Sato, M.; Tokuriki, Y.; Matsumoto, K.; Nakamura, M.  
CS (1) Dep. Neurosurg., Kyoto Univ. Med. Sch., Kyoto Japan  
SO Canadian Journal of Neurological Sciences, (1993) Vol. 20, No. SUPPL. 1, pp. S30.  
Meeting Info.: Vth International Symposium on Cerebral Vasospasm Edmonton and Jasper, Alberta, Canada May 18-21, 1993  
ISSN: 0317-1671.  
DT Conference  
LA English

L6 ANSWER 31 OF 45 CAPLUS COPYRIGHT 2000 ACS  
AN 1993:404342 CAPLUS  
DN 119:4342  
TI Efficacy of futhan rinse solution following rat **heart** preservation  
AU Urushihara, Takashi; Sumimoto, Kazuo; Sumimoto, Ryo; Ikeda, Masanobu; Fukuda, Yasuhiko; Dohi, Kiyohiko  
CS Sch. Med., Hiroshima Univ., Hiroshima, Japan  
SO Nippon Geka Gakkai Zasshi (1992), 93(12), 1514  
CODEN: NGGZAK; ISSN: 0301-4894  
DT Journal  
LA Japanese

L6 ANSWER 32 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1993:288293 BIOSIS  
DN PREV199345006418  
TI Nafamostat mesilate saves the blood loss during open **heart** surgery.  
AU Murase, Mitsuya; Usui, Akihiko; Maeda, Masanobu; Tomita, Yasuhiro; Murakami, Fumihiko; Teranishi, Katuhito; Koyama, Tomio; Abe, Toshio  
CS Nagoya Univ., Nagoya, Aichi Japan  
SO Circulation, (1992) Vol. 86, No. 4 SUPPL. 1, pp. I567.  
Meeting Info.: 65th Scientific Sessions of the American Heart Association New Orleans, Louisiana, USA November 16-19, 1992  
ISSN: 0009-7322.  
DT Conference  
LA English

L6 ANSWER 33 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1992:263628 BIOSIS

DN BA93:139953  
TI EXPERIMENTAL STUDY IN A RABBIT MODEL OF ISCHEMIA-REPERFUSION LUNG INJURY DURING **CARDIOPULMONARY** BYPASS.  
AU KURATANI T; MATSUDA H; SAWA Y; KANEKO M; NAKANO S; KAWASHIMA Y  
CS FIRST DEP. SURG., OSAKA UNIV. MED. SCH., 1-1-50 FUKUSHIMA, FUKUSHIMA-KU, OSAKA 553, JAPAN.  
SO J THORAC CARDIOVASC SURG, (1992) 103 (3), 564-568.  
CODEN: JTCSAQ. ISSN: 0022-5223.  
FS BA; OLD  
LA English

L6 ANSWER 34 OF 45 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2  
AN 1992:248072 CAPLUS  
DN 116:248072  
TI Effect of anticomplement reagents, K-76 COOH and FUT175, on discordant xenograft survival  
AU Miyagawa, S.; Shirakura, R.; Matsumiya, G.; Kitagawa, S.; Fukushima, N.; Nakata, S.; Nakano, S.; Kitamura, H.; Matsumoto, M.; et al.  
CS Med. Sch., Osaka Univ., Osaka, Japan  
SO Transplant. Proc. (1992), 24(2), 483-4  
CODEN: TRPPA8; ISSN: 0041-1345  
DT Journal  
LA English

L6 ANSWER 35 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1992:215286 BIOSIS  
DN BA93:115511  
TI THERAPEUTIC TRIAL OF CEREBRAL VASOSPASM WITH THE SERINE PROTEASE INHIBITOR  
FUT-175 ADMINISTERED IN THE ACUTE STAGE AFTER SUBARACHNOID HEMORRHAGE.  
AU YANAMOTO H; KIKUCHI H; SATO M; SHIMIZU Y; YONEDA S; OKAMOTO S  
CS DEP. NEUROSURGERY, KYOTO UNIV. MED. SCH., KAWAHARA-CHO 54, SYOGGIN, SAKYO-KU, KYOTO, JPN.  
SO NEUROSURGERY (BALTIMORE), (1992) 30 (3), 358-363.  
CODEN: NRSRDY.  
FS BA; OLD  
LA English

L6 ANSWER 36 OF 45 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 3  
AN 1991:526765 CAPLUS  
DN 115:126765  
TI Beneficial effect of therapeutic infusion of nafamostat mesilate (FUT-175)  
on hemodynamics in experimental acute pancreatitis  
AU Dobosz, M.; Sledzinski, Z.; Juszkievicz, P.; Babicki, A.; Stanek, A.; Wajda, Z.; Basinski, A.  
CS 2nd Dep. Gen. Surg., Med. Acad., Gdansk, Pol.  
SO Hepato-Gastroenterology (1991), 38(2), 139-42  
CODEN: HEGAD4; ISSN: 0172-6390  
DT Journal  
LA English

L6 ANSWER 37 OF 45 CAPLUS COPYRIGHT 2000 ACS  
AN 1992:604810 CAPLUS  
DN 117:204810  
TI Combined administration of protease inhibitor and thromboxane A2 synthetase inhibitor for anticoagulation of a left ventricular assist device  
AU Takahama, Tatsuhiko; Kanai, Fukuei; Hiraishi, Mamoru; Onishi, Kiyoshi; Yamazaki, Zenya; Naruse, Yoshihiro; Furuse, Akira; Yoshitake, Tsuyoshi  
CS Saitama Med. Cent., Saitama Med. Coll., Kawagoe, 350, Japan  
SO ASAIO Trans. (1990), 36(3), M141-M144  
CODEN: ASATEJ; ISSN: 0889-7190  
DT Journal  
LA English

L6 ANSWER 38 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
 AN 1990:418614 BIOSIS  
 DN BA90:79415  
 TI EFFECT OF NAFAMOSTAT MESILATE ON SERUM ACTIVITIES OF PANCREATIC ENZYMES AND PLASMA HORMONE LEVELS.  
 AU WAKAYAMA S; SUZUKI T; SAKAI T; MATSUKI A  
 CS DEP. OF ANESTHESIA, AOMORI ROSAI HOSP., HACHINOHE 031, JPN.  
 SO JPN J ANESTHESIOLOGY, (1990) 39 (6), 734-740.  
 CODEN: MASUAC. ISSN: 0021-4892.  
 FS BA; OLD  
 LA Japanese

L6 ANSWER 39 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
 AN 1991:20572 BIOSIS  
 DN BR40:8902  
 TI COMPLEMENT ACTIVATION IN THE ISOLATED **HEART** PROTECTION BY FUT-175 NAFAMOSTAT.  
 AU HOMEISTER J W; SATOH P S; LUCCHESI B R  
 CS UNIV. MICH. MED. SCH., ANN ARBOR, MICH.  
 SO 63RD SCIENTIFIC SESSIONS OF THE AMERICAN HEART ASSOCIATION, DALLAS, TEXAS,  
 USA, NOVEMBER 12-15, 1990. CIRCULATION. (1990) 82 (4 SUPPL 3), III148.  
 CODEN: CIRCAZ. ISSN: 0009-7322.  
 DT Conference  
 FS BR; OLD  
 LA English

L6 ANSWER 40 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
 AN 1989:350455 BIOSIS  
 DN BR37:41552  
 TI PREVENTION OF PULMONARY EDEMA IN AUTOPERFUSING **HEART-LUNG** PREPARATION BY FUT-175 AND LEUKOCYTE DEPLETION.  
 AU NAKA Y; HIROSE H; MATSUDA H; NAKANO S; SHIRAKURA R; KAWAGUCHI A; MIYAMOTO Y; MIYAGAWA S; FUKUSHIMA N; KAWASHIMA Y  
 CS OSAKA UNIV. MED. SCH., FIRST DEP. SURGERY, 1-1-50, FUKUSHIMA, FUKUSHIMA-KU, OSAKA 553, JPN.  
 SO TWELFTH INTERNATIONAL CONGRESS OF THE TRANSPLANTATION SOCIETY, SYDNEY, NEW SOUTH WALES, AUSTRALIA, AUGUST 14-19, 1988. TRANSPLANT PROC. (1989) 21 (1 PART 2), 1353-1356.  
 CODEN: TRPPA8. ISSN: 0041-1345.  
 FS BR; OLD  
 LA English

L6 ANSWER 41 OF 45 CAPLUS COPYRIGHT 2000 ACS  
 AN 1989:546489 CAPLUS  
 DN 111:146489  
 TI Experimental study on the usefulness of the protease inhibitor, nafamostat mesilate (FUT), as an anticoagulant in left **heart** bypass  
 AU Saito, A.; Moro, H.; Eguchi, S.; Yokosawa, T.  
 CS Sch. Med., Niigata Univ., Niigata, Japan  
 SO Jinko Zoki (1989), 18(2), 453-6  
 CODEN: JNZKA7; ISSN: 0300-0818  
 DT Journal  
 LA Japanese

L6 ANSWER 42 OF 45 CAPLUS COPYRIGHT 2000 ACS  
 AN 1988:31609 CAPLUS  
 DN 108:31609  
 TI Comparative study of anticoagulation therapy with an LVAD system  
 AU Takahama, Tatsuhiko; Kanai, Fukuei; Hiraishi, Mamoru; Onishi, Kiyoshi; Yamazaki, Zenya; Furuse, Akira; Asano, Kenichi; Yoshitake, Tsuyoshi  
 CS Saitama Med. Cent., Saitama Med. Coll., Kawagoe, 350, Japan  
 SO ASAIO Trans. (1987), 33(3), 227-34  
 CODEN: ASATEJ; ISSN: 0889-7190

DT Journal  
LA English

L6 ANSWER 43 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1986:16656 BIOSIS  
DN BR30:16656  
TI COMPLEMENT ACTIVATION DURING EXPERIMENTAL **CARDIOPULMONARY** BYPASS  
AND INHIBITORY EFFECT OF FUT-175.  
AU MIYAMOTO Y; HIROSE H; MATSUDA H; NAKANO S; SASAKO Y; NISHIGAKI K; TAKAMI  
H; KAWASHIMA Y; KITAMURA H; NAGAKI K  
SO 22ND ANNUAL MEETING OF THE JAPANESE SOCIETY FOR ARTIFICIAL ORGANS AND  
TISSUES, OSAKA, JAPAN, NOV. 9-10, 1984. ARTIF ORGANS. (1985) 9 (3), 310.  
CODEN: ARORD7. ISSN: 0160-564X.  
DT Conference  
FS BR; OLD  
LA English

L6 ANSWER 44 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1985:235770 BIOSIS  
DN BA79:15766  
TI PHARMACOLOGICAL STUDIES OF FUT-175 NAFAMSTAT MESILATE 1. INHIBITION OF  
PROTEASE ACTIVITY IN-VITRO AND IN-VIVO EXPERIMENTS.  
AU AOYAMA T; INO Y; OZEKI M; ODA M; SATO T; KOSHIYAMA Y; SUZUKI S; FUJITA M  
CS RES. LAB., TORII CO., LTD., 3-14-3 MINAMIYAWATA, ICHIKAWA, CHIBA 272,  
JAPAN.  
SO JPN J PHARMACOL, (1984) 35 (3), 203-228.  
CODEN: JJPAAZ. ISSN: 0021-5198.  
FS BA; OLD  
LA English

L6 ANSWER 45 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1982:267691 BIOSIS  
DN BA74:40171  
TI EFFECTS OF FUT-175 IN ENDO TOXIN SHOCK.  
AU EBATA T; KOBAYASHI K; DENNO R; GOTOH Y; AZUMA K; TOTSUKA M; HAYASAKA H  
CS FIRST DEP. SURGERY, SAPPORO MED. COLLEGE, SAPPORO, 060.  
SO JPN J ANESTHESIOLOGY, (1982) 31 (1), 56-61.  
CODEN: MASUAC. ISSN: 0021-4892.  
FS BA; OLD  
LA Japanese

=> d 6,8,9,13,16 ab,bib

L6 ANSWER 6 OF 45 CAPLUS COPYRIGHT 2000 ACS  
AB It is well known that activation of proteases in the lysosomes and  
cytosol  
is one of the mechanisms of ischemic injury. It might thus be beneficial  
to det. whether the addn. of several clin. available protease inhibitors  
to a **cardioplegic** soln. can improve its protective ability.  
Using an isolated working rat **heart** prepn., the effects of  
several protease inhibitors (serine protease inhibitors; nafamostat  
mesylate and gabexate mesylate, a thiol-protease inhibitor; NCO-700; and  
a urinary trypsin inhibitor, urinastatin) on the postischemic recovery of  
function and enzyme leakage were investigated in this study. These  
protease inhibitors were added to either the **cardioplegic** soln.  
or reperfusion soln. The addn. of each of the protease inhibitors,  
except  
urinastatin, to the **cardioplegic** soln. improved the postischemic  
recovery of function and reduced enzyme leakage. The dose-response  
characteristics of these three protease inhibitors were bell shaped, and  
the optimal concns. of nafamostat mesylate, gabexate mesylate, and  
NCO-700  
were 5 .mu.M, 100 .mu.M, and 20 .mu.M, resp. In contrast to the results



of the preischemic treatment study, the addn. of of the protease inhibitors to the perfusion medium during Langendorff reperfusion failed to improve the postischemic recovery of function and to reduce enzyme leakage. Surprisingly, the addn. of NCO-700 to the reperfusion soln. at

a

concn. of 5 .mu.M or higher had rather harmful effects on both functional recovery and enzyme leakage. These findings suggest that serine and

thiol

proteases may play an important role in myocardial injury during ischemia,

but not necessarily during reperfusion.

AN 1998:183 CAPLUS

DN 128:110669

TI Effects of protease inhibitors on postischemic recovery of the heart

AU Shibata, Toshihiko; Yamamoto, Fumio; Suehiro, Shigefumi; Kinoshita, Hiroaki

CS Second Dep. of Surgery, Osaka City University Medical School, Osaka, 545, Japan

SO Cardiovasc. Drugs Ther. (1997), 11(4), 547-556

CODEN: CDTHET; ISSN: 0920-3206

PB Kluwer Academic Publishers

DT Journal

LA English

L6 ANSWER 8 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS

AB New therapies of cerebral vasospasm aim to prevent the effects of subarachnoid haemorrhage. These effects result in red blood cell haemolysis and release of oxyhaemoglobin, free radicals formation and lipid peroxidations, imbalance in endothelial modulation of vasomotor

tone

and activation of the complement system. Low doses of fibrinolytic agents administered intrathecally accelerate the fibrinolysis of the clot and reduce the oxyhaemoglobin release. The tissue-type plasminogen activator has proven to be effective in preventing vasospasm, but the modalities of this therapy remain to be defined. Free radical reactions may be

inhibited

by free radical scavengers and inhibitors of lipid peroxidations.

Tirilazad

is a potent inhibitor of lipid peroxidations, which improves the patients' outcome and has gone to Phase III human trials. Superoxide dismutase and tropolone derivatives are currently evaluated in animal models. Vasomotor tone can be modified in experimental models either by blocking endothelin receptors (BQ-123), or by facilitating the release and enhancing the effect of nitric oxide using protein kinase C inhibitors, drugs that increase intracellular calcium (cyclopiazonic acid, LP-805) and free radicals scavengers (superoxide dismutase). These possibilities are being investigated. Finally, preliminary studies have demonstrated the efficacy of FUT-175, an inhibitor of the complement system, in the prevention of vasospasm. In the next years, these new therapies have to be validated by prospective and randomized clinical trials to propose guidelines for the management of patients at risk of cerebral vasospasm after aneurysmal rupture.

AN 1996:321861 BIOSIS

DN PREV199699044217

TI Pharmacological therapeutic prospects of cerebral vasospasm.

AU Hans, P.

CS Serv. Univ. d'Anesthesie Reanim., CHR de la Citadelle, 4000 Liege Belgium

SO Annales Francaises d'Anesthesie et de Reanimation, (1996) Vol. 15, No. 3, pp. 374-381.

ISSN: 0750-7658.

DT General Review

LA French

SL French; English

L6 ANSWER 9 OF 45 CAPLUS COPYRIGHT 2000 ACS

AB The effects of nafamostat mesilate (NM) on myocardial, biochem., and functional changes in canine hearts were examd. An isolated heart was preserved for 6 h at 5.degree. and then reperfused for 2 h at 37.degree.. NM was added to the cardioplegic soln. At both 10-7M and 10-6M, NM was able to maintain myocardial cAMP at a normal level and to reduce cGMP concns. at the end of both preservation and reperfusion. The serum N-acetyl-.beta.-D-glucosaminidase concn. during reperfusion was lower in hearts treated with NM 10-6 or 10-7M NM than in those without NM. Although NM failed to preserve myocardial concns. of adenine nucleotide compds., NM at 10-7M maintained the .+-. dp/dt of the left ventricle after reperfusion at the same level as in the nonischemic control group and better than NM at 10-6M or no NM. Myocardial uptake of 10-5M NM was 55% during the 6-h preservation and 29% during the 2-h reperfusion. It is concluded that addn. of 10-7M NM to a nondepolarizing soln. does not preserve myocardial adenine nucleotide concns. but does facilitate the recovery of left ventricular function.

NM at 10-5M seems to have a high affinity for the myocardium and may depress the recovery of left ventricular function.

AN 1997:31579 CAPLUS

DN 126:84283

TI The effect and pharmacokinetics of nafamostat mesilate adjunct to cold nondepolarizing cardioplegia in a canine model of cardiac preservation

AU Sunamori, Makoto; Yoshida, Tetsuya; Miyamoto, Hisashi; Wang, Yigang; Suzuki, Akio

CS School Medicine, Tokyo Medical and Dental University, Tokyo, 113, Japan

SO Transplant Int. (1996), 9(4), 364-369

CODEN: TRINE5; ISSN: 0934-0874

PB Springer

DT Journal

LA English

L6 ANSWER 13 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS

AB In cardiac operations endopeptidase (protease) inhibitor may be beneficial

in reducing myocardial injury when administered in the cardiopulmonary bypass prime. Nafamostat mesilate was evaluated in 20 patients who underwent coronary artery bypass grafting. The patients were divided into a control group (n = 10) and a nafamostat group (n = 10). Nafamostat (2 mg/kg per hour) was continuously given during cardiopulmonary bypass in the nafamostat group. The age, number of grafts, cardiopulmonary bypass time, and aortic crossclamp time were similar between groups. In the control group, neither tumor necrosis factor-alpha nor interleukin-1 levels showed any significant change during

cardiopulmonary bypass, whereas interleukin-6 and interleukin-8 levels, percent expression of adhesion molecule (CD18) on neutrophils, and

CH-50 assay results increased significantly during cardiopulmonary bypass. As compared with the control group, the nafamostat group showed significantly lower levels of interleukin-6 (123 +/- 57 versus 40 +/- 22 pg/ml, respectively,) and interleukin-8 (96 +/- 13 versus 66 +/- 14 pg/ml, respectively). The nafamostat group showed a significantly lower difference of CH-50 assay results and malondialdehyde levels between coronary sinus blood and arterial blood and peak values of creatine

kinase

MB (43 +/- 12 IU/L versus 19 +/- 6 IU/L) during the postoperative course compared with findings in the control group. These results demonstrated that inflammatory reactions induced by cardiopulmonary bypass had adverse effects on myocardial recovery after aortic crossclamping and that nafamostat mesilate given during cardiopulmonary bypass appeared to reduce myocardial reperfusion injury by attenuating such inflammatory reactions. Attenuation of inflammatory reactions of cardiopulmonary bypass should be considered in the strategy of myocardial protection.

AN 1996:112706 BIOSIS  
DN PREV199698684841  
TI Attenuation of **cardiopulmonary** bypass-derived inflammatory reactions reduces myocardial reperfusion injury in cardiac operations.  
AU Sawa, Yoshiki; Shimazaki, Yasuhisa; Kadoba, Keishi; Masai, Takashi; Fukuda, Hirotsugu; Ohata, Toshihiro; Taniguchi, Kazuhiro; Matsuda, Hikaru (1)  
CS (1) First Dep. Surgery, Osaka Univ. Med. Sch., 2-2 Yamada-oka, Suita, Osaka 565 Japan  
SO Journal of Thoracic and Cardiovascular Surgery, (1996) Vol. 111, No. 1, pp. 29-35.  
ISSN: 0022-5223.  
DT Article  
LA English

L6 ANSWER 16 OF 45 BIOSIS COPYRIGHT 2000 BIOSIS  
AN 1995:243942 BIOSIS  
DN PREV199598258242  
TI The anti-complement effects of FUT-175 on myocardial ischemia/reperfusion injury in the blood-perfused isolated rabbit **hearts**.  
AU Yokota, Syunji (1); Kan-No, Satoshi; Saitoh, Yoshiaki; Kasama, Kikuko; Ohara, Naoki; Ono, Hiroshi  
CS (1) Lab. Applied Pharmacology, Hatano Res. Inst., Food Drug Safety Center, Kanagawa 257 Japan  
SO Japanese Journal of Pharmacology, (1995) Vol. 67, No. SUPPL. 1, pp. 280P.  
Meeting Info.: 68th Annual Meeting of the Japanese Pharmacological Society  
Nagoya, Japan March 25-28, 1995  
ISSN: 0021-5198.  
DT Conference  
LA English

=> s myocardial infarction? or stroke? or hemorrhagic shock? or diabetic retinopathy? or venous insufficiency?

L7 399340 MYOCARDIAL INFARCTION? OR STROKE? OR HEMORRHAGIC SHOCK? OR DIABE

CTIC RETINOPATHY? OR VENOUS INSUFFICIENCY?

=> s diabetes?

3 FILES SEARCHED...

L8 320264 DIABETES?

=> s 17 or 18

L9 707481 L7 OR L8

=> s 19 and 11

L10 6 L9 AND L1

=> d 1-6 ab,bib

L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2000 ACS

AB Diagnostic methods that rely on the use of one or more assays that assess cellular activation are provided. The assays are performed on whole blood or leukocytes (neutrophils), and indicate individually or in combination the level of cardiovascular cell activation, which is pivotal in many chronic and acute disease states. These results of the assays are used within a clin. framework to support therapeutic decisions such as:  
further

testing for infectious agents, anti-oxidant or anti-adhesion therapy, postponement and optimal re-scheduling of high-risk surgeries, classifying susceptibility to and progression rates of chronic disease such as **diabetes**, organ rejection, atherogenesis, and **venous insufficiency**; extreme interventions in trauma cases of particularly high risk and activation-lowering therapies. Also provided is compn. derived from a pancreatic homogenate that contains circulating cell activating factors, which can serve as targets for drug screening to identify drug candidates for use in activation lowering therapies. Methods for lowering cell activation by administering protease

inhibitors, particularly serine protease inhibitors, are also provided. Kits for performing the methods are also provided.

AN 1999:595348 CAPLUS  
DN 131:225828  
TI Methods of diagnosis and triage using cell activation measures  
IN Stoughton, Roland B.; Schmid-Schonbein, Geert W.; Hugli, Tony E.; Kistler, Erik  
PA Cell Activation, Inc., USA; The Regents of the University of California; The Scripps Research Institute  
SO PCT Int. Appl., 184 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9946367	A2	19990916	WO 1999-US5247	19990311
	WO 9946367	A3	19991209		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9931829	A1	19990927	AU 1999-31829	19990311
PRAI	US 1998-38894		19980311		
	WO 1999-US5247		19990311		

L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2000 ACS

AB Hypercoagulability is known to occur in the early phase of **hemorrhagic shock**. The prolongation of excessive clot formation after recovery from a shock state leads to the formation of microthrombi or disseminated intravascular coagulation which disturbs microcirculation, damaging organ function. The aim of the present study is to investigate the beneficial effect of a synthetic protease

inhibitor, 6-amidino-2-naphthyl p-guanidinobenzoate dimethanesulfonate (nafamostat mesilate), in the attenuation of hypercoagulability in **hemorrhagic shock**. A model of **hemorrhagic shock** that simulates the clin. course of injured patients was created in anesthetized

dogs. The animals were divided into 2 groups: a control group (group-C) and an exptl. group (group-E). Animals received saline or 0.2 mg/kg of nafamostat mesilate resp., when their mean arterial pressure declined to 50 mmHg. The serum concn. of hydroxytryptamine (5-HT), prothrombin time (PT), and activated partial thromboplastin time (APTT) were detd. as indicators of platelet activity and blood coagulation. In group-C, serum 5-HT was elevated significantly at 60 min after **hemorrhagic shock** but not so in group-E. The APTT at 30 and 60 min was shorter in group-C than in group-E. The PT at 30 min was also shorter in

Yes!  
ordered

group-C. Plasma fibrin degrading products (FDP) increased at 60 min after the induction of shock in group-C. The results indicate that inadequate tissue perfusion in shock stimulates blood coagulation and that

nafamostat

mesilate might be beneficial in decreasing excessive blood coagulation.

AN 1997:186530 CAPLUS

DN 126:233373

TI Nafamostat mesilate, a synthetic protease inhibitor, attenuated hypercoagulability in a canine model of **hemorrhagic shock**

AU Koido, Yuichi; Kato, Kazuyoshi; Shimizu-Suganuma, Masumi; Shichinohe, Kazuhiro

CS Dep. Emerg. Crit. Care Med., Nippon Med. Sch., Tokyo, 113, Japan

SO Nippon Ika Daigaku Zasshi (1997), 64(1), 9-15  
CODEN: NIDZAJ; ISSN: 0048-0444

PB Nippon Ika Daigaku Igakkai

DT Journal

LA English

L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2000 ACS

AB Acute pancreatitis was induced in 13 anesthetized dogs by retrograde injection of bile mixed with trypsin into the pancreatic duct. Six animals were treated with i.v. infusion of new synthetic antiprotease, Nafamostat Mesilate, at a dose of 1 mg/kg/h. Four out of 7 untreated animals died during the expt. All the treated dogs survived.

Hemodynamic

data were regularly monitored during a 10-h observation period. Cardiac output, mean arterial pressure and left ventricular **stroke** vol. decreased rapidly in the untreated animals. ~~An increase in~~ systemic vascular resistance and pulmonary vascular resistance was obsd. in dogs without treatment. Nafamostat Mesilate given as therapy significantly improved the hemodynamic parameters, and prevented the animals from developing shock. The study demonstrates an advantageous influence of synthetic antiprotease Nafamostat Mesilate on the course of acute exptl. pancreatitis.

AN 1991:526765 CAPLUS

DN 115:126765

TI Beneficial effect of therapeutic infusion of nafamostat mesilate (FUT-175)

on hemodynamics in experimental acute pancreatitis

AU Dobosz, M.; Sledzinski, Z.; Juszkiwicz, P.; Babicki, A.; Stanek, A.; Wajda, Z.; Basinski, A.

CS 2nd Dep. Gen. Surg., Med. Acad., Gdansk, Pol.

SO Hepato-Gastroenterology (1991), 38(2), 139-42  
CODEN: HEGAD4; ISSN: 0172-6390

DT Journal

LA English

L10 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS

AB Background: Reperfusion injury in the myocardium has recently been considered to be a type of inflammation, and close attention has been paid

to the possible involvement of neutrophils, complement, and cytokines in the onset of this injury. Recently, it has been reported that serum levels

of interleukin-6 are elevated significantly after **myocardial infarction**. The major site of interleukin-6 production and its exact roles are still unknown. In this study, we hypothesized that myocytes may produce interleukin-6 during hypoxia and this may play a

role

in neutrophil-mediated reperfusion injury. Methods and results: In the clinical study, 20 patients who underwent coronary artery bypass grafting were divided into 2 groups: group F, in which patients were treated with

a

serine protease inhibitor (FUT-175, 2 mg/kg per hour) during cardiopulmonary bypass, and group C (untreated patients). In group C,

YES  
Ordered

myocardial interleukin-6 production, as determined by the difference between the interleukin-6 level in the cardiopulmonary bypass circuit and its level in coronary venous blood, increased significantly after reperfusion (12  $\pm$  4 pg/mL) as compared with that before aortic crossclamping (2  $\pm$  2 pg/mL). In group F, the increase in the interleukin-6 level was suppressed significantly (before aortic crossclamping, 3  $\pm$  2 pg/mL; after reperfusion, 4  $\pm$  3 pg/mL). The interleukin-6 production differed significantly between group C and group F. In the in vitro experimental study, the supernatant from myocytes exposed to 2 hours of hypoxia (group 2H) showed significantly higher levels of interleukin-6 (455  $\pm$  260 pg/mL) than that from normoxic myocytes (group N) (47  $\pm$  15 pg/mL). This interleukin-6 production was suppressed by the addition of FUT-175 (123  $\pm$  24 pg/mL). The

interleukin-6

production by endothelial cells of coronary vessels did not differ between

group 2H (283  $\pm$  151 pg/mL) and group N (151  $\pm$  86 pg/mL). In a coincubation system with a monolayer of endothelial cells on collagen membrane and myocytes under collagen membrane in a modified Boyden chamber, 2 hours of coincubation showed a significantly higher percent of neutrophil transendothelial migration (group 2H vs N, 78%  $\pm$  13% vs 26%

+-

11%), value of chemiluminescence (22  $\pm$  8 vs 5  $\pm$  2  $\times$  10<sup>3</sup> counts/3 minutes), and percent of irreversibly damaged myocytes (48%  $\pm$  17% vs 12%  $\pm$  8%) than normoxic coincubation. In contrast, anti-interleukin-6 monoclonal antibody significantly attenuated neutrophil transendothelial migration (42%  $\pm$  19%) and irreversible damage of myocytes (26%  $\pm$  15%)

in

2 hours of coincubation. Conclusions: Interleukin-6 is produced from myocardium during ischemia and reperfusion in patients undergoing

coronary

bypass grafting. This interleukin-6 may be derived from hypoxic myocytes and play a role in neutrophil-mediated reperfusion injury in myocardium.

AN 1998:475040 BIOSIS

DN PREV199800475040

TI Interleukin-6 derived from hypoxic myocytes promotes neutrophil-mediated reperfusion injury in myocardium.

AU Sawa, Yoshiki (1); Ichikawa, Hajime; Kagisaki, Koji; Ohata, Toshihiro; Matsuda, Hikaru

CS (1) First Dep. Surg., Osaka Univ. Med. Sch., 2-2 Yamada-oka, Suita, Osaka 565 Japan

SO Journal of Thoracic and Cardiovascular Surgery, (Sept., 1998) Vol. 116, No. 3, pp. 511-517.

ISSN: 0022-5223.

DT Article

LA English

L10 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS

AB A 41-year old male with insulin-dependent **diabetes** mellitus previously unsuccessfully treated with a controlled diet and glibenclamide, and subsequently with increasing insulin doses (5 and 20 IU/day) experienced polyuria, glycosuria and loss of weight. On

admittance

to hospital serum C3 concentrations were found to be depressed. The insulin dose was further increased to 30 IU/day and the patient was also treated with 20 mg nafamostat mesylate given intravenously twice daily

for

6 days. On completion of nafamostat mesylate treatment serum C3 concentrations were increased but after 17 days they started to decrease again.

AN 1991:453761 BIOSIS

DN BA92:98541

TI COMPLEMENT ACTIVATION VIA THE ALTERNATIVE PATHWAY IN A PATIENT WITH INSULIN-DEPENDENT **DIABETES** MELLITUS.

AU OKADA S; ICHIKI K; TANOKUCHI S; ISHII K; HAMADA H; YAMAMOTO H; OTA Z

CS THIRD DEP. MED., OKAYAMA UNIV. MED. SCH., 2-5-1 SHIKATA-CHO, OKAYAMA 700,

yes!  
ordered

JPN.  
SO J INT MED RES, (1991) 19 (4), 348-350.  
CODEN: JIMRBV. ISSN: 0300-0605.  
FS BA; OLD  
LA English

L10 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS

AB Sera containing islet cell surface antibody were obtained from seven children with insulin-dependent **diabetes** mellitus soon after the onset of disease. After incubation of 51Cr-labelled rat islet cells with islet cell surface antibody, human AB-type serum with or without nafamostat mesylate was added before further incubation. Radioactivity in the supernatant was measured to determine complement-dependent antibody-mediated cytotoxicity. Cytotoxicity in untreated sera [mean

SD) 19.4  $\pm$  4.0%] was significantly ( $P < 0.001$ ) inhibited by ethyleneglycoltetraacetic acid (EGTA) (7.1  $\pm$  4.9%), ethylene diaminetetraacetic acid (EDTA) (2.5  $\pm$  0.9%) and nafamostat mesylate (2.8  $\pm$  1.8%). Cytotoxicity of nafamostat mesylate-treated serum was significantly ( $P < 0.05$ ) lower than that of EGTA-treated serum but not significantly different from that of EDTA-treated serum. There was no difference in cytotoxicity between nafamostat mesylate-treated and untreated, inactivated human serum. The results indicate that the  
protease

inhibitor nafamostat mesylate completely inhibited the complement activation of the immune complex associated with islet cell surface antibody by the classical and alternative pathways.

AN 1991:365062 BIOSIS

DN BA92:53287

TI DOES PROTEASE INHIBITOR INHIBIT COMPLEMENT ACTIVATION CAUSED BY THE IMMUNE

COMPLEX ASSOCIATED WITH ISLET CELL SURFACE ANTIBODY.

AU OKADA S; SATO K; ICHIKI K; TANOKUCHI S; ISHII K; OTA Z; TAKEDA A

CS THIRD DEP. MED., OKAYAMA UNIV. MED. SCH., OKAYAMA 700, JAPAN.

SO J INT MED RES, (1991) 19 (3), 234-236.

CODEN: JIMRBV. ISSN: 0300-0605.

FS BA; OLD

LA English